The Unethical Use of Placebo

on Vulnerable Human Beings

in High Risk Research

Experiments*

Testimony
To

Committee on Government Reform and Oversight
United States Government
U.S. House of Representative

by

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Dear Mr. Chairman:

I am Adil E. Shamoo from Columbia, Maryland. I am here today to speak on behalf of thousands of vulnerable patients and their families not able or not willing to speak for themselves. I am here to speak on behalf of Citizens for Responsible Care in Psychiatry and Research. As has been mentioned, it was our organization which unearthed the use of fenfluramine on unsuspecting children in New York.

For the purpose of identification only, the following is a brief statement about my background and my involvement in this area.

I am a professor and former chairman of the Department of Biochemistry and Molecular Biology at the University of Maryland, School of Medicine in Baltimore, Maryland. For the past ten years, I have been writing and speaking extensively on issues of ethics in research. I am the editor-in-chief of the journal Accountability in Research, and have chaired five international conferences in the subject.

I would like to thank you Mr. Chairman and members of your Committee for giving me this opportunity to inform you of my personal and my organizations grave concerns regarding the current onaoing research practices of using vulnerable human beings such as the mentally ill and children, as human patients/subjects in high risk experiments on placebo which cause them harm.

Let me state at the outset that we support the use of human subjects in research, but only if their basic human rights are fully respected.

Individuals should only be used as research subjects when it is in their best medical interests. Only under extreme, unique and rare circumstances should we use this population for research without direct medical benefit to them. And only when there is minimal risk involved.

Currently, uncomprehending patients are at the mercy of over zealous psychiatric researchers who claim a "moral imperative" to

conduct high risk, painful experiments on the mentally ill in the name of "science". The attitude of current psychiatric researchers is no different from those who conducted the Tuskegee study. As shocking as it sounds, they believe individual subjects of research must be sacrificed for knowledge that will help future generations.

The Minneapolis Cases

Allow me to give you an example of the neglect that occurs in research on the mentally ill. Imagine, if your daughter or sister or mother who was known for 15 years to be suicidal described to her care givers exactly how she planned to commit suicide. Imagine that you learned she had repeatedly stated that she would commit suicide by jumping off a downtown bridge. Then imagine that your loved one was enrolled in a washout clinical trial for new drug Sertindole to be a part of an FDA drug approval submission. She was enrolled in this study which violated the terms of the protocol which excludes those who are suicidal. She was not monitored by the researchers and proceeded to commit suicide by jumping off the very bridge that she identified to her caregivers. This happened in Minnesota just a few years ago, along with a second suicide, in a study that was regulated by the Food and Drug Administration.

Testimonies of Patients and their Families

On September 18, 1997, patients and families testified before the National Bioethics Advisory Commission (NBAC) that they are victims of therapeutic neglect, betrayal of trust and institutional deception. The patients endured horrendous treatment in ill-conceived, highly speculative, dangerous experiments which clearly undermined the best medical interest of the subjects, often causing them profound harm. Mr. Chairman, many of these experiments are condoned by the FDA and not properly monitored by that agency or any other that has jurisdiction.

These living witnesses represent countless others who have also been harmed and abused in experimental research but who remain silent. The families and patients testified that experiments with large numbers on placebo were conducted without disclosure of known

risks, in other words without informed consent: (1) Consent forms were often presented to subjects who could not understand them, and often presented after the experiments were already under way. (2) Patient records were deliberately changed to fit the experimental protocols. (3) Patients' medical and psychiatric conditions were allowed to deteriorate severely. (4) Patients were subjected to illegal use of restraints. (5) Patients were assaulted and injured by staff. (6) Experimental drug withdrawal procedures led to a suicide attempt (7) One patient on a locked research ward was impregnated and then driven quickly to a clinic outside the institution to obtain an abortion.

I believe this issue is of greater magnitude than the two well known instances in our recent history --namely, the Tuskegee Syphilis study and the radiation exposure experiments.

First, the sheer number of mentally disabled victims who have been used in recent years as I have described, without their informed consent, surpasses the number of those who were victimized in the Tuskegee Syphilis and radiation exposure experiments.

Second, because unethical experiments with vulnerable, mentally disabled human beings are being conducted now, as I speak.

Mr. Chairman, when patients are taken off psychotropic medication to determine whether an investigational drug would be of greater benefit their suffering is substantially greater, than that of most other patients. We need to find a better way to obtain these patients' informed consent. This question is critical, because it is the patients' capacity for self-determination that is affected by their illnesses.

<u>High Risk and Unethical Research with Placebo Protocol</u>

When medications are withdrawn in a research protocol, the relapse rate is as high as 80%. When is the risk to patients considered a sufficient deterrent to the researcher or to the Institutional Review Boards which routinely approve such protocols? A schizophrenia relapse has serious, lasting, harmful consequences for the patient, it can even be life-threatening.

Mr. Chairman, scientists know that in any study there are dropouts, people who suffer consequences of the study and are forced to quit. Thus, it is particularly disturbing that in 88% of the studies we looked at, the researcher failed to report any dropouts from the research protocols, and those that mention dropouts do not indicate the outcome or whereabouts of these subjects.

We also discovered that not a single suicide was reported in 41 US studies of thousands of patients over the past thirty years. This is in contrast to patients' and families recent testimonies that I just cited and the well known fact that suicides among individuals with schizophrenia is very high, about 1% per year.

This of course raises, not only ethical concerns that patients have attempted or succeeded in a suicide and never been reported, but it also raises the issue of the integrity of the research data reported.

Were these suicides or attempted suicides ever reported to IRB's and other officials as required by the regulations? Why have FDA and OPRR not investigated the lack of reported suicides and attempted suicides?

Informed Consent and Comprehension

To illustrate how out of touch the psychiatric community is with the atrocities that they are committing I will read a quote from a recent article:

" *Twenty-eight acutely psychotic patients with schizophrenia* [were the subjects]." "All *of the patients in this study were capable of informed consent and entered voluntarily."* (Barbee et al, 1992). Mr. Chairman, a statement like this is counter-intuitive and plainly absurd.

FDA and Placebo Controls

There is a believe among researcher that drug washout periods and placebo controls were mandated by the Food and Drug Administration (FDA) in drug trial studies. The FDA may come here today and tell this Committee that placebo controlled trials are not required by FDA regulations. But as a matter of standard practice, FDA officials, and specifically Dr. Robert Temple, publish and speak to the scientific community and strongly suggest the need for placebo controlled studies as well as wash out periods where patients are taken off their medication.

Drug companies who invest billions of dollars in research every year know to listen to what Dr. Temple and his colleagues are telling them, if they want their drugs to be approved. And these drug sponsors will continue to design trials with placebo arms that cause undo risk to patients until the FDA changes its approach. By influencing this unethical research FDA has gone far beyond its mandate and is promoting continued suffering among clinical trial subjects.

Recommendations

Mr. Chairman, the exploitation of uncomprehending mentally disabled patients in high risk, non-therapeutic research which offers no direct benefit to its subjects, is a violation of fundamental human rights.

In order to promote the ethical use of vulnerable subjects in research, we offer the following recommendations:

1. **Call for a moratorium on all non-therapeutic, high risk experimentation with placebo control with vulnerable populations and children which is likely to cause a relapse: drug washout and chemically induced relapse studies should be outlawed.**

2. **There should an independent oversight on all research trials involving humans subjects.**

3. **Full disclosure of risks must be enforced.**

4. **A statutory mandate that all clinical trial subjects who suffer adverse consequences during any part of a clinical trial, including the initial wash - out phase be immediately reported to the FDA or other appropriate regulatory agency.**

In closing, we ask the Committee to investigate the unethical exploitation of vulnerable human beings, especially children, who cannot give informed, voluntary or comprehending consent, who are nevertheless subjected to experimental research studies and on placebo which are against their own best interests. We believe that such experiments on non-consensual persons violate fundamental human rights.

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